

Application No. 09/073,596

**Remarks / Arguments**

Claims 82, 84-96, and 98-120 are pending in this application.

Claims 82, 85-88, 90, 93, 96, 98, 100, and 102 have previously been withdrawn from consideration as being drawn to non-elected inventions. However, Applicants retain the right to present these claims in a divisional application.

Claims 99, 101, and 120 have been amended herein to place these claims in better condition for appeal. No new matter has been added by way of these amendments. Support for the recitation of "modified" or "modification" of antigen can be found throughout the specification, *e.g.*, at page 9, line 35 - page 10, line 4, and page 41, lines 29-34. Support for "*in vitro*" cultures and methods can be found throughout the specification, *e.g.*, at page 12, lines 22-25, and at page 41, line 19-22. Support for "enriched and expanded" populations of cells can be found throughout the specification, *e.g.*, at page 41, lines 19-21, and at page 57, lines 20-22.

Thus, after entry of this amendment, claims 84, 89, 91-92, 94-95, 101, and 103-120 will be pending in this application. Applicants respectfully request reconsideration of pending claims 84, 89, 91-92, 94-95, 101 and 103-120.

**I. Rejection Under 35 U.S.C. § 112, Second Paragraph.**

Claim 84 stands rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for recitation of "dendritic cell precursors" (Office Action, paragraph 4).

Applicants respectfully traverse this ground of rejection.

Contrary to the Examiner's assertions, claim 101 (from which claim 84 depends) recites that the antigen-activated dendritic cells are produced from a population of dendritic cell precursors by a given method. Claim 84 recites that these dendritic cell precursors are human.

Thus, Applicants respectfully submit that claim 84 is definite, and meets all the requirements of 35 U.S.C. § 112, second paragraph. Accordingly, Applicants respectfully request that his rejection be reconsidered and withdrawn.

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Claim 115 has also been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for the recitation of "modified antigen," which was lacking antecedent basis in claim 101 (Office Action, paragraph 9)

Claim 101, from which claim 115 depends, has been amended herein to recite "modified" antigen. No new matter has been added by way of this amendment, as support can be found throughout the specification, *e.g.*, at page 9, line 35 - page 10, line 4, and at page 41, lines 29-34.

Accordingly, reconsideration and withdrawal of this ground of rejection is respectfully requested.

II. Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 99, 109, and 116 have been rejected under 35 U.S.C. § 112, first paragraph. The Examiner opines that the specification lacks written description to show the inventors were in possession of the claimed invention at the time the application was filed.

Applicants respectfully traverse this ground of rejection.

A. Claim 99

Claim 99 (as well as independent claim 101) has been amended herein to recite "modified antigen." The Examiner has admitted that support for claim 99 can be found in the specification in the paragraph spanning lines 9-24 on page 42, and specifically lines 22-25 (Office Action, paragraph 11A).

B. Claim 109

Support for the recitation "wherein the cell aggregates are subcultured about one to five times" in claim 109 can be found in originally filed claim 28, and in the paragraph spanning pages 29-30 of the specification.

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C. Claim 116

Support for the recitation of “a pharmaceutical composition comprising a therapeutically effective amount of the composition of claim 101” in claim 116 can be found throughout the specification, *e.g.*, at page 11, lines 8-17, and page 42, lines 14-22.

Thus, Applicants respectfully submit that claims 99, 109, and 116 comply with all the requirements of 35 U.S.C. § 112, first paragraph. Accordingly, Applicants respectfully request that this ground of rejection be reconsidered and withdrawn.

III. Rejection Under 35 U.S.C. § 103(a)

Claims 89, 91-92, 94-95, 97, 99, 101, 103, and 104-120 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Inaba *et al.* (1990), in view of Aldovini *et al.* (1991).

Applicants have amended independent claim 101 (from which all other rejected claims with the exception of claim 120 depend) to recite an *in vitro* composition comprising an enriched and expanded population of antigen-activated dendritic cells presenting modified antigen derived from an *in vitro* culture of an enriched and expanded population of proliferating dendritic cell precursors by a given method.

Applicants have also amended independent claim 120 to recite an *in vitro* composition comprising an enriched and expanded population of antigen-activated dendritic cells derived from an *in vitro* culture of a population of enriched and expanded proliferating precursor cells which were contacted *in vitro* with antigen in the presence of GM-CSF for a sufficient time for antigen modification and presentation to occur.

Inaba *et al.* was cited to teach dendritic cells pulsed with polypeptide or peptide antigens that process and present antigen. However, in fact, Inaba *et al.* states, “As will be evident in Results, it was necessary to expose fresh rather than cultured dendritic cells to a foreign protein to successfully charge these APC with antigen” (page 632, left column, lines 5-7). Inaba *et al.* cultured spleen adherent cells overnight, enriched the dendritic cells, then tested for their capacity to stimulate antigen-primed T cells. Inaba *et al.* concluded that “freshly isolated

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dendritic cells can be successfully pulsed with a variety of soluble protein antigens *in vitro*, but that it is important to administer the antigen shortly after isolating the dendritic cells from the spleen." (page 632, right column, first full paragraph, last sentence).

Thus, Inaba *et al.* actually teaches away from the instant invention of an *in vitro* composition comprising an enriched and expanded population of antigen-activated dendritic cells presenting modified antigen derived from an *in vitro* culture of an enriched and expanded population of proliferating dendritic cell precursors. Accordingly, Inaba *et al.* does not teach or suggest the compositions of the instant invention.

To supplement the deficiency in Inaba *et al.*, the Examiner cites Aldovini *et al.* However, Aldovini *et al.* simply teaches the BCG antigen, and does nothing to supply the deficiency of Inaba *et al.* Moreover, Aldovini *et al.*, either alone or in combination with Inaba *et al.*, does not teach or suggest the compositions of the instant invention.

Furthermore, even if the combination of Inaba *et al.* and Aldovini *et al.* did teach or suggest the composition as recited in independent claim 101 (or the composition of antigen-activated dendritic cells, as recited in new independent claim 120), Applicants respectfully submit that there was no motivation to combine these references. "To establish a *prima facie* case of obviousness based on a combination of the content of various references, there must be some teaching, suggestion or motivation in the prior art to make the specific combination that was made by the applicant." *In re Dance*, 160 F.3d 1339, 1343, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998); *see also In re Dembiczak*, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999) ("Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references."); *In re Fritch*, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992) (modification of the teachings of a prior art reference is not established by the teachings of a second prior art reference "*unless the prior art suggests the desirability of the modification*" (emphasis added)). Thus, Applicants respectfully submit that the motivation to combine the cited references is completely lacking.

Applicants respectfully submit that independent claims 101 and 120, as amended herein, are non-obvious in view of the teachings of Inaba *et al.* and Aldovini *et al.* Similarly, claims 84,

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89, 91-92, 94-95, 97, 99, 101, 103, 104-119, which depend directly or indirectly upon independent claim 101, as amended, thus contain all the limitations thereof, and accordingly also satisfy the requirements of 35 U.S.C. § 103(a).

Thus, reconsideration and withdrawal of this ground of rejection is respectfully requested.

Claim 84 was also rejected under 35 U.S.C. § 103(a) as being unpatentable over Inaba *et al.* (1990) in view of Aldovini *et al.* (1991), as applied above, and in further view of Caux *et al.* (199) as evidenced by Romani *et al.* (1994).

The Inaba *et al.* and Aldovini *et al.* references have been discussed above.

To supplement the deficiencies of Inaba *et al.* and Aldovini *et al.*, the Examiner cites Caux *et al.*, which is said to teach human dendritic cell precursors cultured with GM-CSF and TNF $\alpha$ . Romani was published two years after the earliest priority date claimed in the instant application, and was cited as alleged evidence that culture of CD34+ stem cells in GM-CSF and TNF $\alpha$  will result in "dendritic cell products" (03/14/03 Office Action, paragraph 7, and 07/02/02 Office Action, paragraph 15).

However, Caux *et al.* does not teach an *in vitro* composition comprising an enriched and expanded population of antigen-activated dendritic cells presenting modified antigen derived from an *in vitro* culture of an enriched and expanded population of proliferating dendritic cell precursors, as recited in independent claim 101 (from which claim 84 depends). Thus, Applicants respectfully submit that Caux *et al.* does nothing to supplement the deficiencies in the teachings of Inaba *et al.* and Aldovini *et al.*. Thus, this combination of references does not render independent claim 101, as amended herein, obvious over the cited art. Furthermore, Applicants respectfully submit that the motivation to combine the Inaba *et al.*, Aldovini *et al.*, and Caux *et al.* references is completely lacking.

Applicants respectfully submit that independent claim 101, as amended, satisfies all the requirements of 35 C.F.R. § 103(a). Likewise claim 84, which depends directly upon

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independent claim 101, as amended, thus contains all the limitations thereof, and accordingly, also satisfies the requirements of 35 U.S.C. § 103(a).

Thus, Applicants respectfully request that this ground of rejection be reconsidered and withdrawn.

IV. Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully submit that this application is now in condition for allowance. If a telephone interview would advance prosecution of the application, the Examiner is invited to call the undersigned at the number listed below.

A Petition for a three (3) month Extension of Time under 37 C.F.R. § 1.136(a) is filed concurrently herewith, which extends the response period from 14 May 2003 to 14 August 2003. The Petition further authorizes the PTO to charge the three month extension fee of \$465 to our Deposit Account No. 08-0219, which reflects Applicants' Small Entity Status.

A Notice of Appeal is also filed concurrently herewith, appealing the final rejection as outlined in the 14 February 2003 Final Office Action. The Notice of Appeal further authorizes the PTO to charge the Notice of Appeal fee of \$160 to our Deposit Account No. 08-0219, which reflects Applicant's Small Entity Status.

If there are any other fees due in connection with the filing of these papers, please charge the fees to our Deposit Account No. 08-0219. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above or in the Petition filed concurrently herewith, such an

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extension is requested and the fee should be charged to our Deposit Account. Also, please charge any fees underpaid or credit any fees overpaid to the same Deposit Account.

Respectfully submitted,



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